Remarks

Claims 50-61 are pending in the subject application. By this Amendment, Applicants have amended claims 50 and 54-57 and added new claims 62-65. Support for the amendments and new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, page 100, lines 6-9). Entry and consideration of the new claims and amendments presented herein is respectfully requested. Accordingly, claims 50-65 are currently before the Examiner and favorable consideration of the pending claims is respectfully requested.

Claims 50, and 54-57 have been rejected under 35 U.S.C. §101 on the grounds that the claimed invention is directed to non-statutory subject matter. Specifically, the Office Action argues that the claims fail to recite that the antibody or polypeptide recited in the claim are isolated or purified and, thus, read on proteins found in nature. Applicants note, however, that claim 55 recites a monoclonal antibody, a type of antibody that does not exist in nature and respectfully submit that the rejection is improperly applied as to this claim. Applicants have also amended the independent claim to recite "an isolated" antibody and that this rejection is now moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 50-61 have been rejected under 35 U.S.C. §101 on the grounds that the invention is not supported by a specific asserted utility or a well-established utility. Particularly, the Office Action asserts that the specification and prior art fail to teach the function of the PG1 protein, its association with a specific disease, or its role in the etiology of a specific disease. The Office Action relies upon Xu *et al.* in support of this position, arguing that the reference begins to evaluate the role of PG1 with prostate cancer, but that it has not yet associated or delineated the role of PG1 gene with prostate cancer. The Office Action continues, stating that because Xu et al. represents an initial attempt to equate the PG1 gene with prostate cancer, one cannot be certain that the PG1 gene is, indeed, associated with prostate cancer. Additionally, the Office Action asserts that there is no evidence that the polypeptide to be detected in the claimed invention exists or is expressed. The Office Action also rejects claims 60-61 on the grounds that one skilled in the art would not know how to use the claimed invention because it is not supported by a specific or well-established utility. Applicants note that Xu *et al.* is only directed to linkage and association studies of biallelic markers associated with the PG1 gene and respectfully traverse the rejections on the following grounds.

It is respectfully submitted that *PG1* is associated with prostate cancer. For example, U.S. Patent No. 6,346,381 teaches and claims methods of determining whether an individual is at risk of developing cancer or prostate cancer that comprise the analysis of biallelic markers within the *PG1* gene. As such, the '381 patent clearly provides evidence of the association of the *PG1* gene region with prostate cancer.

It is further submitted that PG1 is expressed in cells and that the Office Action fails to set forth any evidence to the contrary. For example, PG1 expression in host cells transformed with the PG1 polypeptide is taught in Example 7 (beginning at page 54 of the specification). In this example, DNA encoding PG1 and various isoforms of PG1 were fused to a variant of the Green Fluorescent Protein (EGFP) and expressed in normal or adenocarcinoma prostatic cell lines; cells were analyzed for the distribution of the various isoforms of the fusion protein. Normal prostatic cells expressing a truncated form of the PG1 polypeptide (a polypeptide that was identified only in a prostatic tumoural cell line (LNCaP)) showed localization of the polypeptide product only in the cytoplasm of the cell. For full length PG1, localization was observed in, and around, the nucleus of these same cells. Thus, it is respectfully submitted that one skilled in the art would reasonably expect that PG1 polypeptides, as well as various isoforms of the PG1 polypeptide, are expressed in cells and that antibodies to the PG1 polypeptide (or isoforms thereof) would be expected to bind to, and localize, PG1 (or isoforms thereof) expressed in a cell.

The specification also teaches that a variety of splice variants (at least 14 isoforms) of PG1 are observed in a human prostate cDNA library (see Example 8). The specification teaches that at least two splice variants (isoforms containing exon junctions 3-8 and 5-8) were observed in tumoural samples and not in normal samples. Furthermore, certain exon junctions are present in normal samples, but are absent in tumoural samples (for example 2-8, 3b-5, 5b-8). Thus, it is respectfully submitted that the claimed invention has utility in distinguishing between tumorigenic prostate cells and normal prostate cells on the basis of antibody binding to various isoforms of the PG1 polypeptide and that useful information is provided by such binding (for example, by use of antibodies that specifically bind to the splice junctions of the PG1 polypeptide (see specification, page 76, lines 10-31 and the paragraph bridging pages 96-97)). Applicants also submit that the specification also teaches that the art recognizes that alternative splice variants of various proteins

and gene products are associated with various types of cancer (see, for example, page 58, line 6 through page 59, line 23 and page 60, lines 18-21).

Applicants also respectfully submit that the claimed method has a specific asserted utility and/or a well-established utility. For example, the claimed method is useful for the isolation of the PG1 polypeptides via affinity chromatography (see, for example, specification at page 79, lines 7-15). Thus, the claimed method is useful for the isolation of PG1 polypeptide from naturally occurring sources or from cells transformed with nucleic acids encoding PG1 polypeptides, or fragments thereof. The claimed method is also useful for the detection of PG1 polypeptide produced by host cells transformed with polynucleotides that encode the PG1 polypeptide, or fragments of thereof (*e.g.*, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 70 encoding a truncation variant of the PG1 polypeptide (see specification, page 57, lines 19-21)).

U.S. Patent No. 5,945,522 teaches and claims polynucleotide sequences that encode the PG1 polypeptide and transformed host cells containing such nucleic acids. Thus, the claimed methods can be used to identify those cells expressing PG1 and/or to isolate PG1 expressed in the host cells via affinity chromatography as taught in the subject application. Applicants further submit that the claimed methods are also useful in the isolation of polypeptide compositions such as those taught and claimed in U.S. Patent No. 6,265,546 (teaching and claiming compositions comprising a purified or isolated polypeptide comprising a contiguous span of at least 8 amino acids of the PG1 polypeptide (*e.g.*, SEQ ID NO: 4, 5, or 70) or fragments thereof. Another utility of the claimed method includes the detection of truncation variants or splice variants found in tumorous prostatic cells (see, for example, page 57, lines 19-21 disclosing that a truncation variant was identified in prostatic tumoural cell line LNCaP or page 60 disclosing splice variants found only in normal samples or only in tumourous samples). Thus, the claimed method can utilize antibodies that distinguish between the full length PG1 polypeptide and various truncation/splice variants found in normal or tumourous cells.

Applicants further submit that one skilled in the art would know how to use the claimed invention in view of the teachings of the specification. For example, the specification teaches that antibodies to the PG1 polypeptide, splice junctions of the PG1 polypeptide, and isoforms thereof can be made according to methods known in the art (see, for example, pages 75-77; pages 96-100).

Methods of using the antibodies are taught as well. Thus, Applicants respectfully submit that one skilled in the art would recognize the utility of the claimed invention in view of the forgoing arguments and that one skilled in the art would know how to use the claimed invention; accordingly, reconsideration and withdrawal of the utility and enablement rejection set forth in the Office Action of November 19, 2002 is respectfully requested.

The Office Action has also rejected claims 50-61 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Specifically, the Office Action asserts that the recitation of a PG1 polypeptide comprising at least 8 amino acids of SEQ ID NOs: 4, 5, or 70 lack adequate written description in the specification. Applicants respectfully traverse and note that such polypeptide sequences are also the claimed subject matter of U.S. Patent No. 6,265,546.

The Office action has cited to *Fiers v. Revel*, 25 U.S.P.Q.2d 1601 (Fed. Cir. 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), and *The Regents of the University of California v. Eli Lilly*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) in support of its position regarding the written description rejection of record. Applicants respectfully submit that reliance on these cases is improper given the facts of this application. The issue in *Amgen* was whether Amgen's patent was invalid under 35 U.S.C. § 102(g) over prior invention of another. Amgen's patent claimed a purified and isolated DNA sequence encoding human erythropoietin (EPO), *i.e.*, the human EPO gene. Chugai alleged that the invention of Fritsch was conceived prior to Amgen's invention and thereafter diligently reduced to practice by Fritsch. The evidence of record was such that while Fritsch's goal was to obtain the human EPO gene, and he had an idea of a possible method for obtaining it, Fritsch never did isolate the gene, nor identify its structure, and furthermore, others were unsuccessful using Fritsch's approach. The court held that Fritsch's work did not amount to a conception. In Fiers (a three way interference between Fiers, Revel, and Sugano), the interference count was drawn to a DNA coding for human fibroblast interferon-beta polypeptide. The board awarded priority to Sugano, on the ground that Sugano was first to file a patent application that disclosed the gene sequence and a method of making the gene. The Board of Patent Appeals and Interferences held, citing *Amgen*, that Fiers was entitled only to the date of his

British application, because it was the first disclosure (written description) of the complete sequence of the gene by Fiers. In Lilly, a process for producing insulin through a recombinant DNA process was disclosed. While the patent disclosed that the process may be applied to the isolation and purification of the insulin gene from higher organisms generally, including humans, it exemplified, in Example 5, the nucleotide sequence coding for insulin isolated from a rat. No nucleotide sequence information for any other organism was disclosed. The Courts held that the description of a single species of cDNA was insufficient to support the genus claimed in the patent.

Applicants respectfully submit that the facts of the instant application are distinguished from those of the cases cited in support of the instant written description rejection. For example, numerous cDNA encoding various splice variants (isoforms) of the PG1 polypeptide are disclosed in the specification and sequence listing (see, for example, specification, pages 62-64 (SEQ ID NOs: 3, 69, 100-125, 179 and 182-184). The specification and sequence listing also disclose a variety of polypeptides that are encoded by these cDNA isoforms (see, for example, specification at pages 96-97) as well as methods of making such polypeptides; additionally, peptide sequences comprising at least 8 contiguous amino acids encoded over a naturally occurring splice junction site are also taught in the specification (see, for example, pages 76 and 96 of the specification). Thus, it is respectfully submitted that Applicants have taught, disclosed, and provided adequate written description for a number of species of polypeptides within the scope of the instant invention and respectfully submit that the written description aspect of 35 U.S.C. § 112, first paragraph has been met by the application as filed.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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